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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,048	03/31/2004	Bharat Lagu	PRD 2051 NP	7815

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EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	PAPER NUMBER
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,048	LAGU ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *4-6,10,28-36 and 42-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-9,11-27,37-41 and 49* is/are rejected.

7)☒ Claim(s) *48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group I in the reply filed on 11/28/06 is acknowledged. Applicants have additionally elected the first species appearing in claim 48 which corresponds to compound 1 listed on p.61 of the specification . As emphasized in the restriction requirement, within group I directed to the piperazine core, there are many differing fields of search based on the nature of L1 and L2 as well as R3. Further exacerbating the search for the entire set of claims directed to the (elected) piperazine core is the need for separate electronic searches given the multitude of compounds expected to be generated for the basic core which has as the only fixed fragment a phenyl ring attached thereon. A preliminary electronic search for all "L^2" choices with R5 an alkyl group substituted with at least one aryl projected an answer set in the range of about 1900 to 3300 answers. Additionally, differing issues of patentability are expected for the varying "L" choices which can be seen from WO'081 which is relevant to L_2 as $S(O)_2$-R_4 with L^1 as R1b or Chemcat entry cited by applicants which is relevant to L2 as R6-NHC(O). Thus Group I has been further restricted in the following manner.

A. where L2= R3-C(O);

B. where L2= R4S(O)2;

C. where L2= R6-NHC(S);

D. where L2= R6-NHC(O).

Applicants' elected species falls within Group IA. The claims which read on IA subject matter are: 1-3,7-9,11-27,37-41 and 48-49.

Applicants are advised that said claims will be examined fully with respect to the elected species and further to determine patentability of remaining claims.

Claims 7,9,11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. It is not clear in these claims if the first "L" choice is further limiting claim 1 or not. Note the wording "when..." and later "then...." .

Claims 1-3, 7-9, 11-27,38-41 and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specification provides no adequate support teaching how to use representative scope of instant elected piperazine compounds which can

carry from a reading of the specification a huge array of aryl groups as well as heterocyclic groups and heteroaryl at almost every variable including optionally substituted groups thereon as described on pages 41-44. Compounds made do not remotely represent such a scope since all compounds made have the same substitution pattern at R5, i.e. having the benzhydryl group, as well as L1 which is always piperazinylcarbonyl with R3 being phenyl or furyl . "Y" choice is always absent.

Thus, there is no reasonable basis for assuming that the myriad of remaining compounds which easily totals in the billions embraced by the generic claims will all share the same physiological properties since they are so structurally dissimilar as to being chemically and biologically non-equivalent and there is no basis in the prior art for assuming the same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition which include the following factors: 1.) Breadth of the claims- the claims cover compounds easily in the millions if not billions;

2.) Level of unpredictability in the art - the invention is pharmaceutical in nature involving inhibitory activity at the PLC family of proteins. It is well established that the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- as stated above there are only a small number of compounds actually made which are much closer to each other than to remaining scope ;

4) State of the prior art- The compounds are piperazines with phenyl attachment at one end requiring an ortho N-acylated substituent with an additional substituent (L1) and at the other terminus which both can be an array of choices permitted from unsubstituted alkyl to rings that can be mono- and polycyclic. Piperazine carbon atoms can also be further substituted with an assortment of substituted alkyl chains. Note that DuBois's compounds, applied below, embrace a small part of applicants' genus and are taught for treating CCR-3-mediated diseases ;

5) Working examples- While test data has been presented it is limited to a narrow set of homogeneous compounds as described above and thus no

clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 7-9,11-27,37-39 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over DuBois (US'073). DuBois is applied as of its earlier US provisional filing date which precedes applicants' effective filing date since relevant subject matter is described therein. It teaches very similar compounds for use as CCR-3 receptor antagonists. See general formula (I) in col.2 which includes optionally substituted phenyl as "A". Compounds listed in columns 9-14 that pertain to the elected invention, namely #'s 2,5 and 8, only differ in having H in place of instant "L^1" group. Thus the closest instant compounds are methylated vs H in the prior art. H vs Me is not deemed a patentable advance absent evidence of superior, unexpected results. Note In re Wood 199 USPQ 137; In re Lohr 137 USPQ

548; In re Fauque 121 USPQ 425. Additionally, note that DuBois teaches substitution on the phenyl ring at "A" as can be seen in col.7 which includes not only alkyls but substituted alkys as well as carboalkoxy and alkylsufonyl-choices recited herein. Thus it would have been obvious to one skilled in the art at the time the invention was made to modify the closest compounds pointed out above by modifying the phenyl ring with aforementioned substituents and in so doing obtain additional compounds for the uses taught by the art in view of the close structural similarity and equivalency teaching outlined above outlined above.

Claim 48 is objected to for containing nonelected subject matter (see last 7 species), but would otherwise be allowable if limited to elected subject matter of Group IA. DuBois does not teach or suggest the L1 choice as well as R5 choice present in these species.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-

272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E Bernhardt

Emily Bernhardt
Primary Examiner
Art Unit 1624